

Amendments to the Claims

This listing of claims will replace all prior versions

Claims 1-25 (canceled)

Claim 26 (currently amended): A peptide mixture of isolated peptides comprising at least one or more of a first and a second peptide,

wherein said first and said second peptides are two different peptides derived from the hepatitis C virus (HCV), and said first peptide at least one of which is a peptide derived from the C protein of HCV (C peptide) which is selected from the group consisting of:

(a) the peptides consisting of positions 19-47, 27-41, 27-51, 31-57, 104-133, 127-167, 127-149, 131-148, 131-167, 134-148 and 148-167 of the HCV protein,

(b) the peptide consisting of positions 104-133 of the HCV protein and the peptides comprising less than the entire sequence of said peptide and including at least 11 consecutive amino acids of said peptide,

(c) the peptides as defined in (a) or (b) being further modified by substitution of cysteine residues for the alanine residues (C → A) at position +1 or +2, relative to the amino acid residue at the N-terminal position and/or at position -1, -2 or -3, relative to the amino acid residue at the C-terminal position, and

wherein said C peptide ~~that~~ binds with a binding activity <1000 nM to at least four different types of HLA II molecules whose allelic frequency is greater than 5% in the Caucasian population with a binding activity <1000 nM.

Claim 27 (currently amended/withdrawn): The peptide mixture of isolated peptides as claimed in claim 26, further comprising at least one peptide derived from wherein said second peptide is a peptide from the NS3 protein of HCV (NS3 peptide) which is selected from the group consisting of:

(a) the peptides consisting of positions 1007-1037, 1036-1055, 1052-1072, 1076-1093, 1127-1153, 1149-1172, 1174-1195, 1190-1212, 1206-1239, 1246-1275, 1275-1304, 1361-1387, 1377-1403, 1404-1432, 1456-1481, 1495-1513, 1524-1553 and 1552-1583 of the HCV protein,

(b) the peptides comprising less than the entire sequence of the peptides as defined in a) and including at least 11 consecutive amino acids of the peptides as defined in (a),

(c) the peptides as defined in (a) or (b) being further modified by substitution of cysteine residue(s) for the alanine residues (C → A) at position +1 or +2, relative to the amino acid residue at the N-terminal position and/or at position -1, -2 or -3, relative to the amino acid residue at the C-terminal position, and

~~wherein said NS3 peptide that binds with a binding affinity <1000 nM to at least four different types of HLA II molecules whose allelic frequency is greater than 5% in the Caucasian population, with a binding affinity <1000 nM.~~

Claim 28 (currently amended): The ~~peptide~~ mixture of isolated peptides as claimed in claim 26, wherein said HLA II molecules are selected from the group of molecules consisting of HLA-DR1, HLA-DR3, HLA-DR4, HLA-DR7, HLA-DR11, HLA-DR13, HLA-DR15, HLA-DRB3, HLA-DRB4, HLA-DRB5 and HLA-DP4.

Claim 29 (currently amended/withdrawn): The ~~peptide~~ mixture of isolated peptides as claimed in claim 27, wherein said HLA II molecules are selected from the group of molecules consisting of HLA-DR1, HLA-DR3, HLA-DR4, HLA-DR7, HLA-DR11, HLA-DR13, HLA-DR15, HLA-DRB3, HLA-DRB4, HLA-DRB5 and HLA-DP4.

Claim 30 (currently amended): The ~~peptide~~ mixture of isolated peptides as claimed in claim 28, wherein said HLA II molecules are encoded, respectively, by the HLA alleles DRB1*0101, DRB1*0301, DRB1*0401, DRB1*0701, DRB1*1101, DRB1*1301, DRB1*1501, DRB3*0101, DRB4*0101, DRB5*0101, DP*0401 and DP*0402.

Claim 31 (currently amended/withdrawn): The ~~peptide~~ mixture of isolated peptides as claimed in claim 29, wherein said HLA II molecules are encoded, respectively, by the HLA alleles DRB1*0101, DRB1*0301, DRB1*0401, DRB1*0701, DRB1*1101, DRB1*1301, DRB1*1501, DRB3*0101, DRB4*0101, DRB5*0101, DP*0401 and DP*0402.

Claim 32 (canceled)

Claim 33 (canceled)

Claim 34 (currently amended/withdrawn): The ~~peptide~~ mixture of isolated peptides as claimed in claim ~~26~~ 32, wherein the C peptide peptides as defined in (d) ~~are selected from the group consisting of the peptide derived from the C peptide 127-149 of sequence~~ consists of SEQ ID NO: 5.

Claim 35 (canceled)

Claim 36 (currently amended/withdrawn): The peptide mixture of isolated peptides as claimed in claim 27 35, wherein the NS3 peptides of at least 11 amino acids as defined in (b) are selected from the group consisting of:

- the peptides included in peptide 1007-1037 that consist correspond, respectively, to of positions 1007-1021, 1015-1029, 1015-1037, 1019-1033 and 1020-1034 of the HCV protein,
- the peptides included in peptide 1174-1195 that consist correspond, respectively, to of positions 1174-1188, 1174-1192 and 1178-1192 of the HCV protein,
- the peptides included in peptide 1190-1212 that consist correspond, respectively, to of positions 1190-1204 and 1192-1206 of the HCV protein,
- the peptides included in peptide 1246-1275 that consist correspond, respectively, to of positions 1246-1260, 1246-1264, 1250-1264 and 1261-1275 of the HCV protein,
- the peptides included in peptide 1377-1403 that consist correspond, respectively, to of positions 1381-1395, 1381-1397, 1381-1403 and 1383-1397 of the HCV protein,
- the peptide included in the NS3 peptide 1495-1513 that consist corresponds, respectively, to of positions 1495-1509 of the HCV protein,
- the peptides included in peptide 1524-1553 that consist correspond, respectively, to of positions 1524-1552, 1524-1538, 1528-1542, 1528-1552, 1529-1543, 1534-1548, 1538-1552 and 1540-1553 of the HCV protein, and
- the peptides included in peptide 1552-1583 that consist correspond, respectively, to of positions 1559-1573 and 1563-1577 of the HCV protein.

Claim 37 (currently amended/withdrawn): The peptide mixture of isolated peptides as claimed in claim 27 35, wherein the NS3 peptides as defined in c) are selected from the group consisting of the following sequences SEQ ID NO: 10, 13, 20, 22 and 24 and the sequences derived from the sequence of SEQ ID NO:24 that consist correspond, respectively, to of positions 1 to 15, 1 to 29, 5 to 29, 15 to 29 and 17 to 30 of SEQ ID NO: 24 1524-1538, 1524-1552, 1528-1552, 1538-1552 and 1540-1553 of the HCV protein.

Claim 38 (currently amended/withdrawn): The peptide mixture of isolated peptides as claimed in claim 26 27, wherein said first and second peptides include are peptides of derived from the C and NS3 proteins of the hepatitis C virus genotype 1.

Claim 39 (currently amended/withdrawn): The peptide mixture of isolated peptides as claimed in claim 27, which includes wherein 2 to 6 different peptides derived from of the C and NS3 proteins are

included, wherein said ~~all of which~~ peptides altogether bind to at least 10 different types of HLA II molecules whose allelic frequency is greater than 5% in the Caucasian population.

Claim 40 (currently amended/withdrawn): The ~~peptide~~ mixture of isolated peptides as claimed in claim 39, wherein the peptides are selected from the group consisting of the C peptides ~~derived from the C-protein that consist~~ correspond, respectively, of ~~to~~ positions 27-51, 131-167, 127-149, 131-148 and 148-167 of the HCV protein and the NS3 peptides ~~derived from the NS3-protein that consist~~ correspond, respectively, of ~~to~~ positions 1007-1037, 1015-1037, 1036-1055, 1174-1192, 1190-1212, 1246-1264, 1381-1403, 1381-1397, 1524-1553, 1528-1552 and 1552-1583 of the HCV protein.

Claim 41 (currently amended/withdrawn): The ~~peptide~~ mixture of isolated peptides as claimed in claim 27, wherein the peptides are in the form of a single fusion protein comprising [a] the amino acid sequences ~~sequence of the peptides of said mixture, with the exclusion of the sequence corresponding to the fusion of the peptides C 31-45, C 141-155 and NS3 1207-1221 of the HCV protein.~~

Claim 42 (withdrawn): A nucleic acid molecule that encodes a fusion protein as claimed in claim 41.

Claim 43 (withdrawn): A recombinant vector, comprising a nucleic acid molecule as claimed in claim 42.

Claim 44 (withdrawn): A cell that it has been transformed with a vector as claimed in claim 43.

Claim 45 (withdrawn/currently amended): An anti-HCV immunogenic composition, comprising at least one ~~peptide~~ mixture of isolated peptides as claimed in claim 27 in combination with at least one pharmaceutically acceptable vehicle.

Claim 46 (withdrawn): The anti-HCV immunogenic composition as claimed in claim 45 further comprising an adjuvant.

Claim 47 (withdrawn): An anti-HCV immunogenic composition, comprising at least one nucleic acid molecule as claimed in claim 42 in combination with at least one pharmaceutically acceptable vehicle.

Claim 48 (withdrawn): The anti-HCV immunogenic composition as claimed in claim 47 further comprising an adjuvant.

Claim 49 (withdrawn): An anti-HCV immunogenic composition, comprising at least one recombinant vector as claimed in claim 43 in combination with at least one pharmaceutically acceptable vehicle.

Claim 50 (withdrawn): The anti-HCV immunogenic composition as claimed in claim 49 further comprising an adjuvant.

Claim 51 (withdrawn): The immunogenic composition as claimed in claim 45, wherein said peptides are selected from the group consisting of the form of modified peptides, peptides associated with liposomes and peptides associated with lipids.

Claim 52 (withdrawn): The immunogenic composition as claimed in claim 51, wherein said peptide mixture is combined:

- with one or more peptides or lipopeptides containing one or more CD8+ epitopes,
- with other peptides comprising multiple CD4+ epitopes, and/or
- with one or more peptides or lipopeptides containing one or more B epitopes.

Claim 53 (withdrawn): The immunogenic composition as claimed in claim 52, wherein said CD8+ epitopes are selected from the group consisting of the C peptides 2-10, 28-36, 35-44, 41-49, 42-50, 85-98, 88-97, 127-140, 131-140, 132-140, 167-176, 178-187, 181-190; the E1 peptides 220-227, 233-242, 234-242, 363-371; the E2 peptides 401-411, 460-469, 489-496, 569-578, 621-628, 725-733; the NS2 peptides 826-838, 838-845; the NS3 peptides 1073-1081, 1169-1177, 1287-1296, 1395-1403, 1406-1415; the NS4A peptides 1585-1593, 1666-1675; the NS4B peptides 1769-1777, 1789-1797, 1807-1816, 1851-1859; the NS5A peptide 2252-2260 and the NS5B peptides 2588-2596 and 2727-2735 of the HCV protein.

Claim 54 (withdrawn): The immunogenic composition as claimed in claim 52, wherein said CD4+ epitopes are selected from the group consisting of the tetanus toxin TT peptide (positions 830-846), the *Influenza* hemagglutinin HA peptide (positions 307-319), PADRE and the *Plasmodium falciparum* LSA3 peptide.

Claim 55 (withdrawn): The immunogenic composition as claimed in claim 52, wherein said B epitopes are specifically recognized by antibodies directed against either the C peptide 5-27, the NS4 peptide 1698-1719 or the NS5 peptide 2295-2315 of the HCV protein.

Claim 56 (withdrawn): A vaccine comprising an immunogenic composition as claimed in claim 45.

Claim 57 (currently amended): [A] An isolated peptide of the C or NS3 protein of HCV, which is selected from the group consisting of:

(a) the C peptides consisting of positions 19-47, 27-41, 27-51, 31-57, 127-167, 127-149, 131-148, 131-167, 134-148 and 148-167 of the HCV protein the peptides derived from the C-protein of HCV that bind to at least four different HLA II molecules whose allelic frequency is greater than 5% in the Caucasian population with a binding activity <1000 nM, with the exclusion of the peptide C 31-45, C 21-40, C 20-44, C 23-42, C 111-130, C 109-128, C 128-152, C 131-150, C 133-152, C 138-162, C 141-155, C 142-161, C 141-160 and C 145-164,

(b) the C peptide consisting of positions 104-133 of the HCV protein and the peptides comprising less than the entire sequence of said peptide and including at least 11 consecutive amino acids of said peptide

(c) the NS3 peptides derived from the NS3 protein of HCV selected from the group consisting of peptides corresponding, respectively, to consisting of positions 1007-1037, 1036-1055, 1052-1072, 1076-1093, 1127-1153, 1149-1172, 1174-1195, 1190-1212, 1206-1239, 1275-1304, 1361-1387, 1377-1403, 1404-1432, 1456-1481, 1495-1513, 1524-1553 and 1552-1583 of the HCV protein,

(d) the NS3 peptides comprising less than the entire sequence of the peptides as defined in (c) and including of at least 11 consecutive amino acids included in the above of the peptides as defined in (b), with the exclusion of the peptide peptides consisting of positions 1207-1221 and 1384 to 1401 of the HCV protein NS3-1384-1401 and NS3-1207-1221,

(e) the NS3 peptides consisting of positions 1007-1037, 1007-1021, 1015-1029, 1015-1037, 1019-1033, 1246-1275, 1246-1264 and 1261-1275 of the HCV protein, the peptides corresponding, respectively, to positions 1246-1260 and 1261-1275 of the HCV protein, and

(f) the C and NS3 peptides derived from the above peptides as defined in (a) to (e) being further modified by substitution of cysteine residues for the alanine residues (C → A) at positions +1 or +2, relative to the amino acid residue at the N-terminal position and/or at positions -1, -2 or -3, relative to the amino acid residue at the C-terminal position and wherein said C or NS3 peptide as defined in (a) to (e) binds with a binding activity <1000 nM to at least four different types of HLA II molecules whose allelic

frequency is greater than 5% in the Caucasian population.

Claim 58 (previously presented): A diagnostic reagent comprising at least one peptide as claimed in 57 either labeled or complexed in the form of multimeric complexes.

Claim 59 (withdrawn): A method for evaluating the immune state of an individual, comprising detecting the presence of CD4+ T cells specific for HVC peptides by administration of the diagnostic reagent of claim 58 followed by application of an appropriate mechanism adequate for detection of the label or complex.

Claim 60 (withdrawn): A method for sorting HCV-specific T lymphocytes, comprising at least the following steps:

- bringing a suspension of cells to be sorted into contact with one or more labeled tetramers formed from complexes of C and/or NS3 peptides of the HCV protein and with soluble HLA II molecules, and
- separating the cells labeled with the tetramers from the unlabeled cells.

Claim 61 (withdrawn): A method for evaluating the immune state of an individual, comprising detecting the presence of CD4+ T cells specific for HVC peptides by administration of a peptide as defined in claim 26 either labeled or complexed in the form of multimeric complexes followed by detection of the label or complex.

Claim 62 (withdrawn): A method for evaluating the immune state of an individual, comprising detecting the presence of CD4+ T cells specific for HVC peptides by administration of a peptide as defined in claim 27 either labeled or complexed in the form of multimeric complexes followed by detection of the label or complex.

Claim 63 (withdrawn): A method for evaluating the immune state of an individual, comprising detecting the presence of CD4+ T cells specific for HVC peptides by administration of a peptide as defined in claim 26 and detection of the complex formed between CD4+ T cells and said peptide.

Claim 64 (withdrawn): A method for evaluating the immune state of an individual, comprising detecting the presence of CD4+ T cells specific for HVC peptides by administration of a peptide as defined in claim 27 and detection of the complex formed between CD4+ T cells and said peptide.